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(57) Abstract

A method of coating polymeric substrates, especially contact lenses, by reacting functional groups at the substrate polymer surface with complementary functional groups on a hydrophilic coating polymer in an aqueous medium to form covalent linkages between the two polymers. Both polymers are preferably hydrogels. Suitable functional groups include hydroxyl, carboxyl, amino and sulphonate groups. The coating enhances the hydrophilic character of the lens for a longer time relative to an untreated surface, and reduces the tendency for tear proteins to adhere to the lens surface. The coating polymers especially include, among others, polyethylene oxide and polypropylene oxide polymers with pendant functionalities, polydimethylsiloxane graft copolymers with polyethylene oxide, polypropylene oxide, glycidyl acrylate, glycidyl methacylate, epoxypropyl acrylate, or epoxypropyl methacrylate copolymer moieties, and graft copolymers of chitin and chitosan with polyethylene and polypropylene oxide polymers.

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POLYMER COATINGS

This invention relates to the field of polymer coatings. More specifically, it is concerned with coating polymers on to substrates, and embraces methods of coating substrates with polymers, substrates which have been coated by means of the invention, and such coated substrates in the form of contact lenses for the human (or indeed mammalian) eye. Furthermore, to the extent that classes of coating polymer disclosed herein are novel, they and the methods of making them are also within the scope of the invention.

In principle, contact lenses can be made from a wide variety of materials, provided that they meet the necessary requirements for optical clarity, formability and shape stability, non-irritation to the eye, and so on. In practice, contact lenses tend to be made from certain presently preferred materials, including polymers of hydroxyethylmethacrylate (HEMA) and N-vinylpyrrolidone. While these polymerised monomers may make up the bulk of the lens material, say 98%, small amounts of cross-linking agents, such as 2% of ethyl dimethacrylate and 2% of methacrylic acid, may be copolymerised. The lens structure includes voids which are occupied with water, which may make up from typically 38%, up to 60 or 70%, of the total lens weight.

Hydrophilic contact lenses display an affinity for tear calcium and proteins, especially lysozyme, amino acids and glycoproteins, and these readily adhere to the lens surface. It is generally known and accepted that such deposits on contact lenses may cause a decrease in wearing comfort leading to a corresponding decrease in wearing time. Deposits may cause patient's eyes to become infected and it is not uncommon for a subsequent decrease in visual acuity to occur.

Several contact lens care systems have been devised and used for cleaning and disinfecting lenses. Contact lenses with deposits resulting from tear ingredients are usually cleaned with a surfactant cleaner on a daily basis. Soft contact lenses are cleaned additionally with an enzymatic cleaner to remove protein deposits thoroughly. However, even when contact lenses are repeatedly put on and taken off over a period of several months, tear components are sometimes absorbed/adsorbed on the contact lens surface despite use of cleaners.

Soft and hard contact lenses carrying an anionic charge can be complexed with polymers bearing a cationic charge to form a polyelectrolyte complex which reduces the tendency for tear proteins to adhere to a lens surface. However, the interaction between the cationic polymer and the anionic surface of the lens is generally weak, and dissipation of the cationic polymer occurs rapidly in most prior art constructions. As a result, tear proteins are deposited on the lens, and the wearer begins to feel discomfort and must clean the contact lens before rewetting the lens surface with the cationic polymer to form another protective polyelectrolyte complex.

It is an object of this invention to provide the lens surfaces of soft and hard contact lenses, and other substrates, with polymer coatings which are chemically bonded thereto.

In one aspect the invention provides a method of coating a polymeric substrate having functional groups in the substrate polymer chain at surface portions thereof which comprises reacting said functional groups with complementary functional groups on a hydrophilic coating polymer in a predominantly aqueous medium to form covalent linkages between the coating polymer and the substrate polymer. The conditions should be such as to avoid degradation of either polymer.

The coating polymer may be in solution or dispersion in the aqueous

reaction medium. The substrate polymer may advantageously be a hydrogel, that is to say a gel in which the liquid is water. The coating formed on the substrate polymer is also preferably a hydrogel. The coating is desirably continuous.

In a specific embodiment, the invention provides a method of rendering a contact lens that has functional groups (most suitably hydroxyl, carboxyl, amide, amino and sulphonate groups) more compatible with the eye by covalently bonding a polymer to the surface of the lens, which enhances the hydrophilic character of the lens for a longer time relative to an untreated surface, and which reduces the tendency for tear proteins to adhere to the lens surface. The preferred coating polymers are those that form a covalently bound hydrogel at the lens surface, which absorbs water, has good water retention and is compatible with the physiological structure of the eye. Desirably, a durable protective coating is formed which provides long lasting comfort to the eye. The most suitable coatings are hydrophilic and are more resistant to protein deposition than the substrate polymer. Desirable coatings also reduce the deposition of lipids and of ions, such as calcium ions.

The invention also extends, in another aspect, to a substrate polymer coated by the foregoing method, and in particular to a contact lens so coated.

The invention accordingly provides a contact lens, which may comprise a soft or hard contact lens polymer, synthetic or natural, forming the corrective optical element of the lens, having a coating suitable for use in the human eye, wherein the coating comprises a polymer that is covalently bonded to the surface of the lens polymer, thus forming a thin protective layer or coating covalently linked to the lens surface.

In a preferred embodiment a soft or hard contact lens comprises a polymer containing functional groups such as hydroxyl, carboxyl, amide, amino or sulphonic acid, on to which the polymer coating can

be chemically bonded. The functional groups may carry an ionic charge or may have the potential of carrying an ionic charge, for example ions formally derivable by the gain or loss of a proton or electron, or equivalent. Accordingly, references to carboxyl groups and to sulphonic acid groups include carboxylate and sulphonate anions, for example.

Examples of suitable substrate materials include the following polymers with surface functional groups.

Soft hydrophilic contact lens polymer substrates may be crosslinked hydroxyethylmethacrylate (HEMA), crosslinked HEMA and methacrylic acid, and crosslinked HEMA and N-vinylpyrrolidone.

Contact lenses made from natural polymers include cellulose acetate butyrate polymers (retaining free hydroxyl groups).

Contact lenses made from synthetic polymers include polyvinyl alcohol (retaining free hydroxyl groups).

Examples of oxygen permeable hard contact lens polymer substrates include polyfluoroacrylate, polysiloxanyl acrylate and methacrylate polymers, which carry an ionic charge, or retain free hydroxyl groups.

The invention does however extend to the coating of many other polymer substrates with suitable surface functional groups, including those used as contact lens materials, as are well known in the art.

Surprisingly a range of water soluble hydrophilic polymers when covalently bonded to the surface of soft or hard contact lenses provide a hydrophilic surface which reduces the tendency for tear proteins to adhere to a lens surface. These water soluble hydrophilic polymers can be non-ionic and cationic synthetic or natural polymers.

Preferred types of covalent bonding between the respective functional groups on the substrate polymer and the coating polymer include, but are not limited to, carbonate bonding with hydroxyl functional groups on the substrate, ester bonding with carboxyl groups, urethane bonding with amino groups, sulphonic ester bonding with sulphonic acid groups, ether or ester linkages with epoxide groups, urea with hydroxyl groups to form carbamate ester and urea with lens surface carboxyl groups to form acyl carbamate, and amide bonding between an amine and lens carboxyl groups. The reactions between the respective functional groups have as a common feature that they all take place in aqueous media under relatively mild conditions to bind the coating polymer to the substrate surface without degrading either polymer.

Other examples of covalent bonding between functional groups on the respective polymers, in accordance with the invention, include amide, urea, allophanate, biuret, acyl urea and carbodiimide linkages.

Hydrophilic synthetic non-ionic polymers useful as the covalently bound coating polymer include homopolymers, copolymers and graft copolymers of polyvinylalcohol (PVA), homopolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), copolymers of polyethylene oxide and polypropylene oxide, and graft copolymers of siloxanes and polyethylene oxide or polypropylene oxide. Hydrophilic natural polymers useful as the covalently bound coating polymer include homopolymers, copolymers and graft copolymers of cellulose and its derivatives, chitin and chitosan. The following examples of different kinds of polymer are suitable as the coating agent to be covalently bound to the substrate.

Polyvinyl alcohol (PVA) can be covalently bonded to the surface of soft and oxygen permeable hard contact lens to provide a permanent hydrophilic coating which reduces the tendency for tear proteins to adhere to the lens surface.

PVA can be covalently bonded to the surface of a contact lens using conventional water soluble coupling agents or by linking epoxide functionalities on PVA by which it can then be linked to the lens surface.

PVA can be grafted with polyethylene oxide (PEO) or polypropylene oxide (PPO) or a mixture of the two. The graft copolymers can then be covalently bonded to the lens surface using conventional chemistry. In the practice of the invention, PEO and PPO may have the structures shown in Formulae (1) and (2) below :

(1) $X-(CH_2-CH_2-O)_nCH_2-CH_2-Y$ (PEO)

(2) $X-(CH_2-\underset{CH_3}{CH}-O)_nCH_2-\underset{CH_3}{CH}-Y$ (PPO)

where both X and Y can be -OH, $-O-CH_2-CH(NH_2)-CH_3$, $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6, ie including $-O-CO-NH_2$), -COOH, epoxide, $H_2C=CH-CO-O-$ (acrylate), $H_2C=C(CH_3)-CO-O-$ (methacrylate), $-OCH_3$, $-OC_2H_5$, propoxy, butoxy and allyloxy. Compounds in which at least one of X and Y is $-O-CO-(CH_2)_n-NH_2$ are novel.

It is to to be understood that having regard to the inherent asymmetry of PPO (2), the respective terminal X and Y groups can be interchanged in Formula (2).

Molecular weights of (1) and (2) can vary from less than 100 up to 20,000.

Suitable graft copolymers of PVA and PEO, and of PVA and PPO, can also be achieved by reacting PVA with ethylene oxide and propylene oxide respectively, or with a mixture of ethylene oxide and propylene oxide to obtain PVA graft copolymer containing both PEO and PPO. Alternatively instead of ethylene oxide and propylene oxide, ethylene carbonate and propylene carbonate can be used to achieve the same result. The above graft copolymers can then be covalently bonded to the lens surface using conventional chemistry.

Polydimethylsiloxanes can be grafted with (1) or (2) or both through a hydrosilation reaction to form a coating polymer. In (1) and (2), X may be acrylate or methacrylate and Y can be OH, epoxide, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6).

In addition to (1) and (2) being grafted on to polydimethylsiloxanes, glycidyl acrylates (GA), glycidyl methacylates (GM), epoxypropyl acrylate (EPA) and epoxypropyl methacrylate (EPM) may also be grafted, to form a range of novel coating polymers.

The novel polydimethylsiloxane graft copolymers have the following general formula:

$$(CH_3)_3SiO\left[\left((CH_3)_2SiO\right)_x-\left(CH_3\underset{\underset{PEO/PPO/GA/GM/EPA/EPM}{|}}{Si}O\right)_y\right]_n Si(CH_3)_3$$

The coefficients x, y and n can vary to give molecular weights in a broad range of 3000 to 100,000.

The above water soluble hydrophilic polymers may be covalently bonded to the lens surface using conventional chemistry.

Ethylene oxide and propylene oxide can react with cellulose to produce graft copolymers of PEO-cellulose and PPO-cellulose, or a mixture of ethylene oxide and propylene oxide may be used to give PEO/PPO-cellulose graft copolymer. The same result can also be achieved by using ethylene carbonate and propylene carbonate. Analogous results are achieved with hydroxyethyl cellulose in place of cellulose

Alternatively, (1) and (2) can be grafted on to hydroxyethylcellulose and then covalently bonded to the surface of the contact lens.

Hydroxyethyl cellulose can also have epoxide functionalities through which it can be covalently bonded using conventional water soluble coupling agents.

Chitin and chitosan can also be grafted with PEO and PPO using ethylene oxide and propylene oxide or a mixture of both to form a further range of novel coating polymers. The graft copolymers may then be covalently bonded to the lens surface.

Soft and oxygen permeable hard contact lenses can also be made more resistant to tear protein deposition by directly polymerising ethylene oxide or propylene oxide or a mixture of the two on to the contact lens. Alternatively, PEO and/or PPO may be grafted directly on to the lens surface. The same results can be achieved by using ethylene carbonate and/or propylene carbonate instead of ethylene and propylene oxides.

Homopolymers of (1) and (2) can also be used to covalently bond to the contact lens surface to provide a hydrophilic coating which reduces the tendency of tear proteins to deposit on to the lens surface.

For such homopolymers of (1) and (2), X can be either acrylate or methacrylate and Y can be OH, COOH, epoxide, OCH_3, OC_2H_5, propoxy, butoxy, allyloxy, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6).

In (1) and (2), the presence of the vinyl double bond when X is acrylate or methacrylate enables the molecule to be homopolymerised to produce polymers with pendant OH, COOH, epoxide, OCH_3, OC_2H_5, propoxy, butoxy, allyloxy, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$, or a mixture of pendant groups. For example, if (1) in which X is acrylate and Y is OH is polymerised then all pendant groups will be OH. However, if it is polymerised with another molecule, where X is the same but Y is an epoxide or any of the other pendant groups, then a mixture of two pendant groups is achieved. The mixture need

not be limited to a mixture of two pendant groups, but can be more than two.

Similarly (1) and (2) can be copolymerised when X is either methacrylate or acrylate and Y for both (1) and (2) can be the same or different groups.

Both (1) and (2) can also be copolymerised with a variety of unsaturated monomers when X for (1) and (2) is either methacrylate or acrylate and Y can be any of OH, COOH, epoxide, OCH_3, OC_2H_5, propoxy, butoxy, allyloxy, $-O-CH_2-CH(NH_2)-CH_3$, and $-O-CO-(CH_2)_n-NH_2$. Suitable unsaturated monomers for co-polymerisation include vinylene carbonate, hydroxyethylmethacrylate, hydroxypropylmethacrylate, hydroxyethyl acrylate, hydroxypropylacrylate, n-vinylpyrrolidone, acrylamide, hydroxybutylacrylate, hydroxybutylmethacrylate, butylacrylamide, dihydroxypropylacrylate, dihydroxypropylmethacrylate, epoxypropyl-acrylate, epoxypropylmethacrylate, glycidyl acrylate, glycidyl methacrylate, and hydroxypropylmethacrylamide.

Synthetic cationic polymers which can be covalently bonded to the lens surface include cationic PVA, and copolymers of polyethylene oxide and polypropylene oxide. In such copolymers, with reference to Formulae (1) and (2), X may be acrylate or methacrylate and Y can be OH, epoxide, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6). (1) and (2) can then be copolymerised with :

(a) (1) or (2) where X is acrylate or methacrylate Y can be $OCH_2N(CH_2)_2$, $OCH_2N^+(CH_3)_3.Cl^-$, $OCH_2N^+(C_2H_5)_3.Cl^-$, $OCH_2CH_2N(CH_2)_2$, $OCH_2CH_2N^+(CH_3)_3.Cl^-$, $OCH_2CH_2N^+(C_2H_5)_3.Cl^-$, $OCH_2CH_2CH_2N(CH_2)_2$, $OCH_2CH_2CH_2N^+(CH_3)_3.Cl^-$, $OCH_2CH_2CH_2N^+(C_2H_5)_3.Cl^-$, $OCH(OH)CH_2CH_2N^+(CH_3)_3.Cl^-$ or $OCH_2CH(OH)CH_2N^+(CH_3)_3.Cl^-$

(b) other cationic polymerisable monomers which include : dimethylaminoethyl acrylate and methacrylate, 2-methacryloyl-oxyethyltrimethylammonium chloride, 3-methacrylamidopropyl

dimethylamine, 3-methacrylamidopropyl trimethylammonium chloride, 1-vinyl and 2-methyl 1-vinylimidazole, 3-acrylamido-3-methylbutyl-dimethylamine, 3-acrylamido-3-methylbutyl trimethylammonium chloride, N-(3-methacryloyloxy-2-hydroxypropyl) trimethylammonium chloride, diallyldimethylammonium chloride and methylsulphate, vinylbenzyltrimethylammonium chloride.

In addition to the grafting species for polydimethylsiloxanes given earlier for the covalent linkage of non-ionic graft copolymers of polydimethylsiloxanes to the substrate polymer, all grafting monomers given in (a) and (b) above may also be used to provide cationic graft copolymers of polydimethylsiloxanes.

Cationic natural polymers which may be covalently bonded to a substrate such as a lens surface include cationic cellulose and chitosan.

The invention is further illustrated in the following examples.

Example 1

Coating a substrate with PVA-PEO graft copolymer - Formula (1), X and Y both OH. Molecular weight ca. 600.

14g PEO was dissolved in anhydrous acetone. 3.3g carbonyl diimidazole (CDI) was also dissolved in anhydrous acetone and placed in a dry dropping funnel. The CDI was added dropwise to the PEO over a period of one hour. The solution was left to stir for a further one hour after which the acetone was evaporated off under reduced pressure.

3g PVA (25,000 M.Wt) was dissolved in 40mM potassium bicarbonate buffer (pH 8.5) with boiling. When the solution had cooled, CDI-activated PEO was added and the mixture was magnetically stirred for twenty-four hours. The solution was next dialysed for

twenty-four hours, then the resultant PVA-PEO graft copolymer was freeze dried.

The copolymer was dissolved in anhydrous dimethylsulphoxide (DMSO). CDI (3.3g) was dissolved in DMSO and added dropwise over a period of one hour. The solution was further stirred for one hour before the DMSO was distilled off under reduced pressure.

Three high water content contact lenses of polyhydroxyethyl-methacrylate (polyHEMA) containing methacrylic acid were washed in water and each of them placed in 5ml of potassium bicarbonate buffer (40mM, pH 8.5). To each of the lenses 150mg of CDI-activated PVA-PEO graft copolymer was added and left for twenty-four hours. PVA-PEO graft copolymer was linked to the surface via carbonate bonds to surface OH groups and via ester bonds to surface COOH groups. The contact lenses were removed, washed in water and placed in phosphate buffered saline (PBS) (10mM, pH 7.4).

Protein absorption studies

Analysis of protein film deposits on the lenses after human wear indicate that the film consists primarily of denatured lysozyme. Since lysozyme comprises only 18 per cent of the total tear proteins, it appears to be selectively absorbed and denatured on the surfaces of soft hydrophilic lenses.

Lysozyme absorption studies were carried out by incubating the lens in 5ml of lysozyme solution for approximately twenty-four hours. 0.05% w/v lysozyme was dissolved in PBS. After twenty-four hours the lysozyme solution was measured spectrophotometrically at 281.6nm. Control solutions contained untreated contact lenses.

The results showed that there was a 90% reduction in lysozyme absorption when compared against the untreated lenses.

Example 2

Coating a substrate with PVA-PEO graft copolymer - Formula (1), X is OH and Y $-OCH_3$. PEO molecular weight ranged from 300 to 5000.

As in Example 1, the PEO was activated with CDI (mole ratio 1:1) in acetone and reacted with PVA in 40mM potassium bicarbonate buffer (pH 8.5) for twenty-four hours. The solution was next dialysed for twenty-four hours, then the resultant PVA-PEO graft copolymer was freeze dried.

The copolymer was dissolved in anhydrous acetone. CDI (3.3g) was dissolved in acetone and added dropwise over a period of one hour. The solution was further stirred for one hour before the acetone was distilled off under reduced pressure.

As in Example 1, three high water content polyHEMA contact lenses were treated with 150mg of the CDI-activated PVA-PEO graft copolymer. The graft copolymer was linked to surface OH groups via a carbonate linkage and to surface COOH groups via an ester linkage.

Lysozyme absorption studies showed that after treatment there was a 90% reduction in lysozyme absorption relative to the control untreated lens.

Example 3

PVO-PEO graft copolymers were synthesised as in Example 2. The graft copolymer was linked to the lens surface using a water soluble carbodiimide (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride) (EDC).

Three high water content polyHEMA contact lenses were each placed in 5ml distilled water (pH 6) containing 20mg EDC and incubated at

room temperature for six hours. To this solution 150mg of PVA-PEO graft copolymer was added and the temperature of the solution was gradually raised to 80°C over a period of one hour and maintained at 80°C for two hours. The graft copolymer was linked to the lens surface COOH groups via an ester linkage.

Lysozyme absorption studies showed that after treatment there was a 90% reduction in lysozyme absorption relative to the control.

Example 4

Coating a substrate with PVA-PEO graft copolymer - Formula (1), X being OH and Y epoxide. Molecular weight 1000.

3g PVA (25000 M.Wt) was dissolved in distilled water (100ml) with boiling. When the solution had cooled, 20g PEO and 2ml NaOH (1M) were added. The solution was left stirring for twenty-four hours at room temperature. The solution was neutralised with 1M HCl and then dialysed for twenty-four hours and freeze dried.

The resultant graft copolymer of PVA-PEO was either dissolved in 100ml anhydrous acetone or anhydrous DMSO to which was added 3.3g CDI dissolved in either acetone or DMSO over a period of one hour. The solution was left stirring for another hour and then the solvent was removed under reduced pressure.

As in Example 1, three high water content polyHEMA contact lenses were treated with 150mg of the CDI-activated PVA-PEO graft copolymer. The graft copolymer was linked to surface OH groups via a carbonate bond and to surface COOH groups via an ester linkage.

Lysozyme absorption studies showed that after treatment there was a 90% reduction in lysozyme absorption relative to the control untreated lens.

Example 5

3g PVA (25000 M.Wt) was dissolved in 100ml distilled water after boiling. 2ml of NaOH (1M) was added to the cooled solution. Ethylene oxide was cooled to below 0° C and poured into the vessel, and the vessel temperature was maintained at approximately 2° C. The reaction was stopped when PVA could be dissolved in acetone.

The solution was neutralised, dialysed for twenty-four hours and freeze dried. PVA-PEO graft copolymer was dissolved in acetone and activated with CDI (3.3g).

Soft high water content polyHEMA lenses (as in Example 1) were incubated with 150mg of the polymer. The graft copolymer was covalently bonded to the lens surface. The graft copolymer formed a carbonate bond with surface OH groups and an ester linkage with surface COOH.

Protein absorption studies showed a 95% reduction in lysozyme absorption relative to untreated contact lenses.

Example 6

Polydimethylsiloxanes grafted with PEO (Formula (1), Y being OH) also showed greater than 90% reduction in lysozyme absorption when the polymers were covalently bonded to the lens surface of high water content polyHEMA contact lenses using CDI.

PEO molecular weights ranged from 350-2500 and the overall graft copolymer molecular weight of polydimethylsiloxanes and PEO ranged from 4000-30,000. All or half PEO hydroxyl groups were activated on the polymers with CDI in acetone, before linking to the lens surface took place in potassium bicarbonate buffer. The PEO hydroxyl groups which were activated with CDI reacted with the lens surface hydroxyl groups to form a carbonate bond and also formed

ester linkages with surface COOH groups.

Example 7

Polydimethylsiloxanes grafted with PEO (Formula (1), Y being OH) and glycidylacrylate, the molecular weight of the graft copolymers being in the range 5000-10000, were incubated with soft high water content polyHEMA lenses (as in Example 1) in the presence of a Lewis acid. The cocktail contained one contact lens in 5ml distilled water with 250mg graft copolymer and 0.5ml Lewis acid. The solution was left at room temperature for twenty-four hours. The graft copolymer was covalently bound to the lens surface via the epoxide group on the glycidylacrylate. The epoxide formed an ether linkage with surface OH groups and an ester linkage with surface COOH groups.

both polyHEMA and the oxygen permeable hard lenses.

The lenses were tested for lysozyme absorption. Greater than 90% reduction in lysozyme absorption was observed for both types of lenses.

Example 9

High water content polyHEMA and oxygen permeable hard contact lenses (polysiloxanyl methacrylate copolymerised with methacrylic acid) were placed in vials. To each of these vials 5ml distilled water was added and 250mg ethylene carbonate. Potassium carbonate (50mg) was added and the solution warmed to ca. 60°C for two hours. Ethylene carbonate reacted with the lens surface to form polyethylene oxide polymer on both lens types. However, the initial bond with the lens surface is dependent on the functional group present. If OH is present, the initial bond is an ether linkage, and if COOH is present, then an initial ester bond is formed.

The lenses were washed and tested for lysozyme absorption. Greater than 90% reduction in protein absorption was observed for the treated lenses when compared to control untreated lenses.

Example 10

Coating a substrate with PEO polymer - Formula (1), X is OH and Y $-OCH_3$. PEO polymers of molecular weights between 200 and 5000 were used, including molecular weights of 200, 350, 550, 750, 1000, 2000 and 5000.

CDI was dissolved in anhydrous acetone. PEO was also dissolved in anhydrous acetone and placed in a dry dropping funnel. The PEO was added dropwise to the CDI over a period of one hour. The solution

was left to stir for a further one hour, after which the acetone was evaporated off under reduced pressure. Mole ratio 1:1 was used to obtain CDI-activated PEO polymer.

As in Example 1, three high water content polyHEMA contact lenses were treated with 200mg of the CDI-activated PEO polymer. The polymer was linked to surface OH groups via a carbonate linkage and to surface COOH groups via an ester linkage.

Lysozyme and albumin absorption studies showed that after treatment there was 90% reduction in lysozyme and albumin absorption relative to the control untreated lens.

Example 11

Coating a substrate with PEO polymers - Formula (1), X is OH and Y is (a) OH and (b) $-OCH_3$. PEO polymers with molecular weights of between 200 and 20000 were used, including 200, 550, 750, 1000, 2000, 5000, 10000 and 20000.

As in Example 3, three high water content contact lenses were each placed in 5ml distilled water (pH 6) containing 20mg EDC and incubated at room temperature for six hours. To this solution 400mg PEO polymer was added and the temperature of the solution was gradually raised to 80°C over a period of one hour and maintained at 80°C for two hours.

The polymer was linked to the lens surface COOH groups via an e. er linkage.

Example 12

Coating a substrate with PEO polymer - Formula (1), X is $-OCH_2-\underset{\underset{CH_3}{|}}{C}NH_2$

and Y $-OCH_3$. Molecular weights of the PEO polymer varied from 200 to 10000.

As in Example 10, the PEO polymer was activated with CDI and reacted with three high water content polyHEMA contact lenses and three oxygen permeable hard contact lenses (as in Example 8). In the polyHEMA lens, the chemical bond was a urethane linkage with lens surface OH groups and an amide linkage with surface COOH for both polyHEMA and the oxygen permeable hard lens.

The lenses were tested for both lysozyme and albumin absorption. Greater than 90% reduction in lysozyme and albumin was observed for both types of lenses.

Example 13

Coating a substrate with PEO polymer - Formula (1), X is $-OCH_2-\underset{\underset{CH_3}{|}}{C}NH_2$

and Y $-OCH_3$. Molecular weights of the PEO polymer varied from 200 to 10000.

As in Example 3, EDC was used to couple the PEO polymer to the lens COOH groups, but instead of forming an ester linkage (as in Example 3) an amide bond was formed.

Lysozyme and albumin studies showed that after treatment there was a 90% reduction in lysozyme and albumin relative to the control.

Example 14

Coating a substrate with PEO polymer - Formula (1), X is $-O-\overset{\overset{O}{\|}}{C}-NH_2$ and Y is (a) OH, (b) $-OCH_3$ and (c) $-O-\overset{\overset{O}{\|}}{C}-NH_2$

Molecular weights of the PEO polymer varied from 200 to 20000.

The above polymer is formed by reacting a PEO polymer (Formula 1) where X is OH and Y is OH or $-OCH_3$ with urea. PEO polymer and urea are refluxed for six hours in an organic solvent (dioxane or toluene).

The organic solvent is removed under reduced pressure. The resultant PEO polymer is then linked to the surface of the contact lens either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond formed with lens surface OH groups was a carbamate ester and an acyl carbamate with lens COOH groups. Similarly, with EDC the bond formed is also a carbamate ester with lens COOH groups.

Lysozyme studies showed that after treatment there was a 90% reduction in lysozyme absorption relative to the control untreated lens.

Example 15

Coating a substrate with PEO polymers.

(i) Formula (1), X is methacrylate and Y is OH. Molecular weight of PEO polymer can vary between 200 and 2000.

The above PEO polymer was homo-polymerised in water. 90 wt% distilled water was de-gassed and purged with nitrogen for half an

hour and then heated to 80°C. PEO polymer (10 wt%) containing 230mg potassium persulphate (dissolved in 2ml distilled water) was added slowly to the heated water (under nitrogen) over a period of fifteen minutes. The reaction was allowed to continue for one hour. The polymer was then dialysed for twenty-four hours and freeze dried.

(ii) Formula (1), X is methacrylate and Y is $-OCH_3$. Molecular weight of PEO polymer can vary between 200 and 5000.

Co-polymerisation of PEO polymers in (i) and (ii) was carried out with different mole ratios and different molecular weights. Examples of copolymers of (i) and (ii) are given in Table 1.

Table 1

	Mole %
(i) Molecular weight 350, 550, 750, 1000	10, 20, 30, 40, 50, 60, 70, 80, 90, 100
(ii) Molecular weight 350, 550, 750, 1000, 2000	90, 80, 70, 60, 50, 40, 30, 20, 10, 0

The polymers in Table 1 were then linked to the surface of polyHEMA high water content contact lenses either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond was a carbonate with lens surface OH groups and an ester with surface COOH groups. With EDC the chemical bond was an ester with surface COOH groups.

Example 16

Coating a substrate with PEO polymers - Formula (1) where X is methacrylate and Y is $-O-\overset{\overset{O}{\|}}{C}-NH_2$

The above PEO polymer was synthesised as described below. A mole ratio of 1:1 of urea and PEO polymer - Formula (1), X is methacrylate and Y is OH (molecular weight 350) was refluxed for six hours in anhydrous dioxane or toluene. The solvent was then removed under reduced pressure. Similarly, other molecular weights of Formula (1), where X is methacrylate and Y is OH were reacted with urea (eg molecular weights 550, 750 and 1000).

The above PEO polymers were then either homo-polymerised or copolymerised with :

(a) Formula (1), where X is methacrylate and Y is OH, molecular weights 350, 550 and 750.

(b) Formula (1), where X is methacrylate and Y is $-OCH_3$, molecular weights 350, 550, 750, 1000 and 2000.

(c) A mixture of PEO polymers in (a) and (b).

The polymers were then linked to the surface of polyHEMA high water content contact lenses either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond was a carbamate ester with lens surface OH groups and an acyl carbamate with surface COOH groups. With EDC the chemical bond was also an acyl carbamate with surface COOH groups.

Lysozyme and albumin studies showed that after treatment there was a 90% reduction in lysozyme and albumin absorption relative to the control untreated lens.

Example 17

Acrylamide and methacrylamide were (separately) copolymerised (as in Example 15) with:

(a) Formula (1), where X is methacrylate and Y is OH, molecular weights 350, 550 and 750.

(b) Formula (1), where X is methacrylate and Y is $-OCH_3$, molecular weights 350, 550, 750, 1000 and 2000.

(c) A mixture of (a) and (b).

The mole % of acrylamide varied between 10 and 90 mol% in the above polymerisation mixtures.

The polymers were linked to the surface of polyHEMA high water content contact lenses either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond was a carbonate bond between polymer OH groups and lens surface OH groups or a carbamate ester with acrylamide or methacrylamide. An ester bond was formed between polymer OH groups and lens surface COOH groups or an acyl carbamate with acrylamide or methacrylamide. With EDC the chemical bond was either an ester between polymer OH groups and lens surface COOH groups or an acyl carbamate with acrylamide or methacrylamide with lens surface COOH groups.

Lysozyme and albumin studies showed that after treatment there was a 95% reduction in lysozyme and albumin absorption relative to the control untreated lens.

Example 18

Vinylene carbonate (mol% 20, 40 and 60) was copolymerised (as in Example 15) with PEO polymer Formula (1), where X is methacrylate

and Y is $-OCH_3$, molecular weight 350. Similarly vinylene carbonate (mol% 20, 40 and 60) was copolymerised with other molecular weight PEO polymers of the above structure (eg 550, 750, 1000 and 2000).

Vinylene carbonate (mol% 20, 40 and 60) was also copolymerised with PEO polymer Formula (1), where X is methacrylate and Y is OH, molecular weight 350.

The above polymers were dialysed for twenty-four hours and freeze dried.

Polymerisation reactions of the above copolymers were also carried out in organic solvents such as toluene and isopropanol under nitrogen using VAZO 67 (du Pont) (2,2-azobis(2-methylbutane-nitrile)) as catalyst. The mixtures were allowed to reflux for twenty-four hours, after which the solvent was removed under reduced pressure.

Three high water content polyHEMA contact lenses were placed in potassium carbonate (pH 9.0) and 300mg of one of the above polymers was added.

The polymers were linked to the lens surface OH groups via an ether linkage and to the lens COOH groups via an ester linkage.

Lysozyme and albumin studies showed that after treatment there was an 85% reduction in lysozyme and albumin absorption relative to the control untreated lens.

Example 19

Glycidyl methacrylate (mol% 20, 40 and 60) was copolymerised (as in Example 15) with PEO polymer Formula (1), where X is methacrylate and Y is $-OCH_3$, molecular weight 350. Similarly glycidyl methacrylate (mol% 20, 40 and 60) was copolymerised with other

molecular weight PEO polymers of the above structure (eg molecular weights 550, 750, 1000 and 2000).

Glycidyl methacrylate (mol% 20, 40 and 60) was also copolymerised with PEO polymer Formula (1), where X is methacrylate and Y is OH molecular weights 350 and 550.

In addition, 40 mol% glycidyl methacrylate was copolymerised with 30 mol% PEO polymer - Formula (1), where X is methacrylate and Y is $-OCH_3$ (molecular weight 2000) and 30 mol% PEO polymer - Formula (1), where X is methacrylate and Y is OH (molecular weight 350).

The above polymers were dialysed for twenty-four hours and freeze dried.

Polymerisation reactions of the above copolymers were also carried out in organic solvents such as toluene under nitrogen using VAZO 67 (du Pont) as catalyst. The mixtures were allowed to reflux for twenty-four hours, after which the solvent was removed under reduced pressure.

Three high water content polyHEMA contact lenses were placed in distilled water (pH 10) and 300mg of one of the above polymers was added. The polymers were linked to the lens surface OH groups via an ether linkage and to the lens COOH groups via an ester linkage.

Lysozyme studies showed that after treatment there was an 85% reduction in lysozyme absorption relative to the control untreated lens.

Example 20

N-vinyl pyrrolidone (mol% 20, 40 and 60) was copolymerised (as in Example 15) with PEO polymer - Formula (1), where X is methacrylate and Y is $-OCH_3$, molecular weight 350. Similarly N-vinyl pyrrolidone (mol% 20, 40 and 60) was copolymerised with other

molecular weight PEO polymers of the above structure (eg molecular weights 550 and 750).

The above polymers were dialysed for twenty-four hours and freeze dried.

The polymers were then linked to the surface of polyHEMA high water content contact lenses either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond was a carbonate with lens surface OH groups and an ester with surface COOH groups. With EDC the chemical bond was an ester with surface COOH groups.

Lysozyme studies showed that after treatment there was an 80% reduction in lysozyme absorption relative to the control untreated lens.

Example 21

Hydroxyethylmethacrylate (HEMA) (mol% 20, 40 and 60) was copolymerised (as in Example 15) with PEO polymer - Formula (1), where X is methacrylate and Y is $-OCH_3$, molecular weight 350. Similarly, HEMA (mol% 20, 40, and 60) was copolymerised with other molecular weight PEO polymers of the above structure (eg molecular weights 550, 750, 1000 and 2000).

The above polymers were dialysed for twenty-four hours and freeze dried.

The polymers were then linked to the surface of polyHEMA high water content contact lenses either by using CDI (as in Example 10) or by using EDC (as in Example 3). With CDI the chemical bond was a carbonate with lens surface OH groups and an ester with surface COOH groups. With EDC the chemical bond was an ester with surface COOH groups.

Lysozyme studies showed that after treatment there was an 85% reduction in lysozyme absorption relative to the control untreated lens.

Example 22

2-methacryloyloxyethyltrimethylammonium chloride (mol% 10, 20 and 30) was copolymerised (as in Example 15) with PEO polymer - Formula (1), where X is methacrylate and Y is OH (molecular weight 350). Similarly the above cationic monomer was copolymerised with other molecular weight PEO polymers of the above structure (eg molecular weights 550 and 750).

The cationic monomer was also copolymerised with 40mol% PEO polymer - Formula (1), where X is methacrylate and Y is OH (molecular weight 350) and 30mol% PEO polymer - Formula (1), where X is methacrylate and Y is $-OCH_3$ (molecular weight 2000).

The above copolymers were dialysed for twenty-four hours and freeze dried.

The polymers were then linked to the surface of polyHEMA high water content contact lenses by using EDC (as in Example 3). The chemical bond was an ester with surface COOH groups.

Lysozyme studies showed that after treatment there was an 85% reduction in lysozyme absorption relative to the control untreated lens.

Example 23

Cationic PVA (molecular weight 25000) (200mg) was linked to the surface of a polyHEMA high water content contact lens by using EDC (as in Example 3). The chemical bond was an ester with surface COOH groups.

Lysozyme studies showed that after treatment there was an 80% reduction in lysozyme absorption relative to the control untreated lens.

Example 24

Cationic cellulose (molecular weight 50000) was linked to the surface of a polyHEMA contact lens in an identical fashion to that in Example 23, and similar reductions in lysozyme absorption were observed relative to the untreated control.

CLAIMS

1. A method of coating a polymeric substrate having functional groups in the substrate polymer chain at surface portions thereof which comprises reacting said functional groups with complementary functional groups on a hydrophilic coating polymer in a predominantly aqueous medium to form covalent linkages between the coating polymer and the substrate polymer.

2. A method according to claim 1 wherein the substrate polymer is a hydrogel.

3. A method according to claim 1 or claim 2 wherein the coating formed on the substrate polymer is a hydrogel.

4. A method according to any one of the preceding claims wherein the coating is continuous.

5. A method according to any one of the preceding claims wherein the substrate material is selected from crosslinked hydroxyethylmethacrylate (HEMA), crosslinked HEMA and methacrylic acid, crosslinked HEMA and N-vinylpyrrolidone, cellulose acetate butyrate polymers (retaining free hydroxyl groups), polyvinyl alcohol (retaining free hydroxyl groups), polyfluoroacrylate, polysiloxanyl acrylate and methacrylate polymers carrying an ionic charge or retaining free hydroxyl groups.

6. A method according to any one of the preceding claims wherein the covalent bonding between the respective functional groups on the substrate polymer and the coating polymer is selected from carbonate bonding with hydroxyl functional groups on the substrate, ester bonding with carboxyl groups, urethane bonding with amino groups, sulphonic ester bonding with sulphonic acid groups, ether and ester linkages with epoxide groups, urea with hydroxyl groups

to form carbamate ester and urea with substrate surface carboxyl groups to form acyl carbamate, and amide bonding between an amine and substrate carboxyl groups.

7. A method according to any one of the preceding claims wherein the covalent bonding between the respective functional groups on the substrate polymer and the coating polymer is selected from amide, urea, allophanate, biuret, acyl urea and carbodiimide linkages.

8. A method according to any one of the preceding claims wherein the covalently bound coating polymer is a hydrophilic polymer selected from homopolymers, copolymers and graft copolymers of polyvinylalcohol (PVA), homopolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), copolymers of polyethylene oxide and polypropylene oxide, graft copolymers of siloxanes, and homopolymers, copolymers and graft copolymers of cellulose, chitin and chitosan.

9. A method according to claim 8 wherein the coating polymer comprises a graft copolymer of PVA with PEO or PPO or a mixture of the two covalently bonded to the substrate.

10. A method according to claim 9 wherein the graft copolymer of PVA and PEO, or of PVA and PPO, is achieved by reacting PVA with ethylene oxide or ethylene carbonate, or propylene oxide or propylene carbonate, respectively, or with a mixture thereof, to obtain PVA graft copolymer containing PEO and/or PPO.

11. A method according to any one of claims 8 to 10 wherein the PEO and PPO have the structures shown in Formulae (1) and (2) below:

(1) $X-(CH_2-CH_2-O)_nCH_2-CH_2-Y$ (PEO)

(2) $X-(CH_2-\underset{CH_3}{CH}-O)_nCH_2-\underset{CH_3}{CH}-Y$ (PPO)

where both X and Y are -OH, $-O-CH_2-CH(NH_2)-CH_3$, $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), -COOH, epoxide, $H_2C=CH-CO-O-$ (acrylate), $H_2C=C(CH_3)-CO-O-$ (methacrylate), $-OCH_3$, $-OC_2H_5$, propoxy, butoxy or allyloxy, and the respective terminal X and Y groups can be interchanged in Formula (2).

12. A method according to claim 11 wherein the molecular weights of (1) and (2) are from less than 100 up to 20,000.

13. A method according to claim 8 wherein the coating polymer is a graft copolymer of a polydimethylsiloxane with (1) or (2) or both, wherein X is acrylate or methacrylate and Y is OH, epoxide, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6).

14. A method according to claim 8 wherein the coating polymer is a graft copolymer of a polydimethylsiloxane with a glycidyl acrylate (GA), a glycidyl methacylate (GM), an epoxypropyl acrylate (EPA), or an epoxypropyl methacrylate (EPM).

15. A method according to claim 8 wherein the coating polymer comprises a homopolymer of PEO or PPO of Formula (1) or (2) respectively.

16. A method according to claim 15 wherein the coating polymer comprises a homopolymer of PEO or PPO of Formula (1) or (2) respectively wherein X is either acrylate or methacrylate and Y is OH, COOH, epoxide, OCH_3, OC_2H_5, propoxy, butoxy, allyloxy, $-O-CH_2-CH(NH_2)-CH_3$, $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6).

17. A method according to claim 8 wherein the coating polymer comprises a copolymer of PEO and PPO of Formula (1) and (2) respectively wherein X is either methacrylate or acrylate and Y for (1) and (2) can be the same or different groups.

18. A method according to claim 17 wherein X is either methacrylate or acrylate and Y is any of OH, COOH, epoxide, OCH_3, OC_2H_5, propoxy, butoxy, allyloxy, $-O-CH_2-CH(NH_2)-CH_3$, and $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), with an unsaturated monomer selected from vinylene carbonate, hydroxyethylmethacrylate, hydroxypropylmethacrylate, hydroxyethyl acrylate, hydroxypropylacrylate, N-vinylpyrrolidone, acrylamide, hydroxybutylacrylate, hydroxybutylmethacrylate, butylacrylamide, dihydroxypropylacrylate, dihydroxypropylmethacrylate, epoxypropylacrylate, epoxypropylmethacrylate, glycidyl acrylate, glycidyl methacrylate, and hydroxypropylmethacrylamide.

19. A method according to claim 8 wherein the coating polymer is selected from cationic PVA and synthetic cationic copolymers of polyethylene oxide and polypropylene oxide.

20. A method according to claim 19 wherein the coating polymer is a copolymer of a polydimethylsiloxane or of PEO or PPO of Formula (1) or (2), wherein X is acrylate or methacrylate and Y is OH, epoxide, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), with PEO or PPO of Formula (1) or (2) where X is acrylate or methacrylate and Y is $-OCH_2N(CH_2)_2$, $-OCH_2N^+(CH_3)_3.Cl^-$, $-OCH_2N^+(C_2H_5)_3.Cl^-$, $-OCH_2CH_2N(CH_2)_2$, $-OCH_2CH_2N^+(CH_3)_3.Cl^-$, $-OCH_2CH_2N^+(C_2H_5)_3.Cl^-$, $-OCH_2CH_2CH_2N(CH_2)_2$, $-OCH_2CH_2CH_2N^+(CH_3)_3.Cl^-$, $-OCH_2CH_2CH_2N^+(C_2H_5)_3.Cl^-$, $-OCH(OH)CH_2CH_2N^+(CH_3)_3.Cl^-$ or $-OCH_2CH(OH)CH_2N^+(CH_3)_3.Cl^-$

21. A method according to claim 19 wherein the coating polymer is a copolymer of a polydimethylsiloxane or of PEO or PPO of Formula (1) or (2), wherein X is acrylate or methacrylate and Y is OH, epoxide, $-O-CH_2-CH(NH_2)-CH_3$, or $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), with another cationic polymerisable monomer selected from dimethylaminoethyl acrylate and methacrylate, 2-methacryloyl-oxyethyltrimethylammonium chloride, 3-methacrylamidopropyl dimethylamine, 3-methacrylamidopropyl trimethylammonium chloride, 1-vinyl and 2-methyl 1-vinylimidazole, 3-acrylamido-3-methylbutyl-

dimethylamine, 3-acrylamido-3-methylbutyl trimethylammonium chloride, N-(3-methacryloyloxy-2-hydroxypropyl) trimethylammonium chloride, diallyldimethylammonium chloride and methylsulphate, and vinylbenzyltrimethylammonium chloride.

22. A substrate polymer coated by a method according to any one of the preceding claims.

23. Polyethylene oxide (PEO) and polypropylene oxide (PPO) having a structure as shown in Formula (1) or (2) below:

(1) $X-(CH_2-CH_2-O)_nCH_2-CH_2-Y$ (PEO)

(2) $X-(CH_2-\underset{CH_3}{CH}-O)_nCH_2-\underset{CH_3}{CH}-Y$ (PPO)

where one of X and Y is $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), and the other is $-OH$, $-O-CH_2-CH(NH_2)-CH_3$, $-O-CO-(CH_2)_n-NH_2$ (where n is from 0 to 6), $-COOH$, epoxide, $H_2C=CH-CO-O-$ (acrylate), $H_2C=C(CH_3)-CO-O-$ (methacrylate), $-OCH_3$, $-OC_2H_5$, propoxy, butoxy or allyloxy.

24. Polydimethylsiloxane graft copolymers having the following general formula:

$$(CH_3)_3SiO\left[((CH_3)_2SiO)_x-(\underset{PEO/PPO/GA/GM/EPA/EPM}{CH_3SiO})_y\right]_n-Si(CH_3)_3$$

where PEO/PPO/GA/GM/EPA/EPM represents polyethylene oxide, polypropylene oxide, glycidyl acrylate, glycidyl methacylate, epoxypropyl acrylate, or epoxypropyl methacrylate copolymer moieties, and the coefficients x, y and n are such as to give a molecular weight in the broad range of 3000 to 100,000.

25. Graft copolymers of chitin and chitosan with PEO and PPO.

26. A method of increasing the resistance of soft and oxygen permeable hard contact lenses to tear protein deposition comprising directly polymerising ethylene oxide or ethylene carbonate, or propylene oxide or propylene carbonate, or a mixture thereof, on to the contact lens, or by grafting PEO and/or PPO directly on to the lens surface.

27. A method of rendering a contact lens that has functional groups more compatible with the eye, comprising covalently bonding a polymer coating to the surface of the lens as a substrate, whereby to enhance the hydrophilic character of the lens for a longer time relative to an untreated surface, and to reduce the tendency of tear proteins to adhere to the lens surface.

28. A method according to claim 27 wherein the functional groups are hydroxyl, carboxyl, amide, amino or sulphonate groups.

29. A method according to claim 27 or claim 28 wherein the coating polymer forms a covalently bound hydrogel at the lens surface.

30. A contact lens coated by a method according to any one of claims 26 to 29.

31. A contact lens having a coating suitable for use in the human eye, wherein the coating comprises a polymer that is covalently bonded to the surface of the lens polymer to form a thin protective layer or coating covalently linked to the lens surface.

32. A contact lens according to claim 31 which comprises a polymer containing hydroxyl, carboxyl, amide, amino or sulphonic acid functional groups on to which the polymer coating is chemically bonded.

INTERNATIONAL SEARCH REPORT

International application No. PCT/GB 92/00901

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.5 C 08 J 7/04 G 02 B 1/04 A 61 L 27/00

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl.5	C 08 J G 02 B A 61 L

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
X	WO,A,9000887 (BIOMETRIC SYSTEMS INC.) 8 February 1990, see claims 1-9,12-15,38-40; page 2, paragraph 3; page 3, paragraph 1, page 6, paragraphs 1,2; pages 7-9; page 12, paragraph 2; pages 20-21 ---	1,8
X	US,A,4373009 (R. ALASTAIR WINN) 8 February 1983, see claims 1,2,3,8,9,19,20,27,48; column 2, lines 45-65; column 5, lines 1-33; column 5, lins 51-55 ---	1-4
X	FR,A,2649404 (UNIVERSAL HIGH TECHNOLOGIES) 11 January 1991, see claims 1-9; page 5, lines 2-17: page 9, lines 19-22 --- -/-	1

° Special categories of cited documents :[10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
17-07-1992	19. 10. 92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	DEPIJPER R.D.C.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X	EP,A,0187137 (SCHERING CORP.) 9 July 1986, see claims 1,4-7; page 21, example 8; page 22, example 9	1
A	EP,A,0026660 (MONSANTO CO.) 8 April 1981, see claims 1,6-11; page 2, line 21 - page 3, line 24	1
A	DE,A,2748256 (BAUSCH & LOMB INC.) 3 May 1978, see claims 1-17; page 8, paragraph 3 - page 9, paragraph 1	1
A	US,A,4921497 (JIRI SULC) 1 May 1990, see claims 1,2	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB92/00901

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claims 1 - 22, 26 - 32
2. Claim 23
3. Claim 24
4. Claim 25

For further information please see Form PCT/ISA/206 mailed 10/08/92

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently this international search report is restricted to the invention first mentioned in the claims; ~~it is covered by claims~~

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9200901 SA 59363

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 14/10/92 The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A- 9000887	08-02-90	EP-A- 0425485	08-05-91
		US-A- 5002582	26-03-91
US-A- 4373009	08-02-83	AU-B- 556584	13-11-86
		AU-A- 8947382	03-05-84
		EP-A,B 0106004	25-04-84
		GB-A,B 2128500	02-05-84
		JP-B- 3077819	11-12-91
		JP-A- 59081341	11-05-84
FR-A- 2649404	11-01-91	US-A- 4801475	31-01-89
		DE-A- 3529758	27-02-86
		FR-A- 2569374	28-02-86
		GB-A,B 2163436	26-02-86
		US-A- 4959074	25-09-90
		US-A- 5037677	06-08-91
		US-A- 5023114	11-06-91
EP-A- 0187137	09-07-86	AU-B- 569649	11-02-88
		AU-A- 5179286	10-07-86
		CA-A- 1273537	04-09-90
		JP-B- 1058486	12-12-89
		JP-C- 1572962	20-08-90
		JP-A- 61182013	14-08-86
		US-A- 4668240	26-05-87
EP-A- 0026660	08-04-81	US-A- 4277541	07-07-81
		AU-B- 531153	11-08-83
		AU-A- 6282780	09-04-81
		CA-A- 1139074	11-01-83
		JP-A- 56057835	20-05-81
DE-A- 2748256	03-05-78	US-A- 4143949	13-03-79
		CA-A- 1074254	25-03-80
		GB-A- 1579469	19-11-80
		JP-A- 53083642	24-07-78
US-A- 4921497	01-05-90	AU-A- 2663788	15-06-89
		DE-A- 3841380	22-06-89

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9200901 SA 59363

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 14/10/92
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 4921497		FR-A- 2624515	16-06-89
		GB-A,B 2213489	16-08-89
		GB-A- 2243612	06-11-91
		JP-A- 1279933	10-11-89
		US-A- 5080683	14-01-92